IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Mapleson *et al.* Atty. Dkt. No.: 1324.024A

Serial No.: Unknown
Continuation of 09/463,762
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Group Art Unit: 1645
Examiner: Fields, I.

Title: METHOD OF REMOVING ENDOTOXIN FROM VACCINES

Assistant Commissioner for Patents
Box Patent Application
Washington, D.C. 20231

PRELIMINARY AMENDMENT UNDER 37 CFR 1.115

Dear Sir:

This document accompanies a filing under 37 CFR 1.53(b). Prior to calculation of the filing fee, and prior to examination of the application, please amend the priority application as follows:

Amendment

Please amend the application as follows:

In the specification:

Page 1, after the title and prior to the first paragraph, insert:

Prior Foreign Applications

This application is a continuation of United States Patent Application Serial Number 09/463,762, filed April 27, 2000 as a 35 USC §371 filing of International Patent Application Number PCT/GB98/02314, filed July 31, 1998 and claims priority from GB Patent Application Number 9716242.4, filed July 31, 1997. The entire disclosures of the earlier applications are incorporated herein by reference.

Field of the Invention

Page 1, between the first and second paragraphs, insert:

Background of the Invention

Page 4, following the last full paragraph and prior to "It is an object . . .", insert:

Summary of the Invention

Page 9, following the first full paragraph and prior to "Figure 1 illustrates . . .", insert:

Detailed Description of the Preferred Embodiments

After the claims, insert the attached new page 21, which contains the following text:

Abstract of the Invention

A method of removing bacterial endotoxin from a pharmaceutical process solution is disclosed. In one embodiment, the method comprises treating the solution with a surfactant effective to dissociate the endotoxin from a pharmaceutical drug or vaccine substance in the solution, and then filtering the solution through a molecular cut-off filter having a pore size effective to retain the pharmaceutical drug or vaccine substance but allow the dissociated bacterial endotoxin to pass therethrough.

In the claims:

I. Canceled claims

Please cancel claim 6 without prejudice.

II. Amended claims

Please amend claims 3-4, 7-9, 12, 14 and 17-18 to read as follows:

3. A method according to claim 2 wherein the amphiphilic pharmaceutical drug or vaccine substance comprises a glycoprotein.

4. A method according to claim 1 wherein the amphiphilic drug or vaccine substance is a vaccine antigen.

7. A method according to claim 5 wherein the antigen is an influenza antigen.

8. A method according to claim 5 wherein the antigen is a haemagglutinin and/or neuraminidase antigen.

9. A method according to claim 1 wherein the surfactant is an anionic surfactant.

12. A method according to claim 11 wherein the surfactant is a salt selected from the group consisting of salts of deoxycholate, cholate, glycocholate, taurodeoxycholate and taurocholate.

14. A method according to claim 1 wherein the surfactant is present at a concentration which is at least as great as the critical micelle concentration of the surfactant.

17. A method according to claim 1 wherein the molecular weight cut-off filter comprises a regenerated cellulose acetate membrane, or a polysulphone membrane.

18. A method according to claim 1 wherein, following removal of the bacterial endotoxin, the process solution is subjected to a further process step in which the surfactant is removed.

The amended claims effect the following changes:

3. (once amended) A method according to [claim 1 or] claim 2 wherein the amphiphilic pharmaceutical drug or vaccine substance comprises a glycoprotein.

4. (once amended) A method according to [any one of the preceding claims] **claim 1** wherein the amphiphilic drug or vaccine substance is a vaccine antigen.

7. (once amended) A method according to claim 5 [or claim 6] wherein the antigen is an influenza antigen.

8. (once amended) A method according to [any one of claims 5 to 7] **claim 5** wherein the antigen is a haemagglutinin and/or neuraminidase antigen.

9. (once amended) A method according to [any one of the preceding claims] **claim 1** wherein the surfactant is an anionic surfactant.

12. (once amended) A method according to claim 11 wherein the surfactant is a salt **selected from the group consisting of salts** of deoxycholate, cholate, glycocholate, taurodeoxycholate [or] **and** taurocholate.

14. (once amended) A method according to [any one of the preceding claims] **claim 1** wherein the surfactant is present at a concentration which is at least as great as the critical micelle concentration of the surfactant.

17. (once amended) A method according to [any one of the preceding claims] **claim 1** wherein the [a] molecular weight cut-off filter comprises a regenerated cellulose acetate membrane, or a polysulphone membrane.

18. (once amended) A method according to [any one of the preceding claims] **claim 1** wherein, following removal of the bacterial endotoxin, the process solution is subjected to a further process step in which the surfactant is removed.

III. New claim

Please add claim 20.

20. A method according to claim 7 wherein the antigen is a haemagglutinin and/or neuraminidase antigen.

Remarks

Following International prosecution, the priority PCT application included claims 1-19. As claim 6 has been canceled and claim 20 has been added herein, claims 1-5 and 7-20 are pending in this continuation.

The claim amendments remove multiple dependency; no new matter has been added. Applicants respectfully request examination and consideration of claims 1-5 and 7-20.

Respectfully submitted,

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